Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Vildagliptin/Metformin 50mg/1000mg film-coated tablets

vildagliptin & metformin hydrochloride

PL 55863/0076

Novumgen Limited

LAY SUMMARY

Vildagliptin/Metformin 50mg/1000mg film-coated tablets
vildagliptin & metformin hydrochloride

This is a summary of the Public Assessment Report (PAR) for Vildagliptin/Metformin 50mg/1000mg film-coated tablets. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Vildagliptin/Metformin in this lay summary for ease of reading.

For practical information about using Vildagliptin/Metformin, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Vildagliptin/Metformin and what is it used for?
This product is a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised, called Eucreas 50 mg / 1000 mg film-coated tablets (PLGB 00101/1045).

Vildagliptin/Metformin tablets are used to treat adult patients with type 2 diabetes. This type of diabetes is also known as non-insulin-dependent diabetes mellitus. Vildagliptin/Metformin tablets are used when diabetes cannot be controlled by diet and exercise alone and/or with other medicines used to treat diabetes (sulphonylureas).

Type 2 diabetes develops if the body does not make enough insulin or if the insulin that the body makes does not work as well as it should. It can also develop if the body produces too much glucagon.

Both insulin and glucagon are made in the pancreas. Insulin helps to lower the level of sugar in the blood, especially after meals. Glucagon triggers the liver to make sugar, causing the blood sugar level to rise.

How does Vildagliptin/Metformin work?
The active substances of Vildagliptin/Metformin tablets, vildagliptin and metformin, belong to a group of medicines called “oral antidiabetics”. Both active substances, vildagliptin and metformin, help to control the level of sugar in the blood. The substance vildagliptin works by making the pancreas produce more insulin and less glucagon. The substance metformin works by helping the body to make better use of insulin. This medicine has been shown to reduce blood sugar, which may help to prevent complications from diabetes.

How is Vildagliptin/Metformin used?
The pharmaceutical form of these medicines is a film-coated tablet and the route of administration is oral (by mouth).

The amount of Vildagliptin/Metformin that people have to take varies depending on their condition. The patient’s doctor will tell them exactly the dose of Vildagliptin/Metformin to take.

The recommended dose is one film-coated tablet of 50 mg/1000 mg taken twice a day.

If the patient has reduced kidney function, their doctor may prescribe a lower dose. Also, if the patient is taking an anti-diabetic medicine known as a sulphonylurea their doctor may prescribe a lower dose.

The patient's doctor may prescribe this medicine alone or with certain other medicines that lower the level of sugar in the blood.

When and how to take Vildagliptin/Metformin

- The patient should swallow the tablets whole with a glass of water.
- The patient should take one tablet in the morning and the other in the evening with or just after food. Taking the tablet just after food will lower the risk of an upset stomach.

The patient should continue to follow any advice about diet that their doctor has given them. In particular, if the patient is following a diabetic weight control diet, they should continue with this while they are taking Vildagliptin/Metformin.

For further information on how Vildagliptin/Metformin is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Vildagliptin/Metformin have been shown in studies?

Because Vildagliptin/Metformin is a generic medicine, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Vildagliptin/Metformin?

For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Vildagliptin/Metformin is a generic medicine and is bioequivalent to the reference medicine, its benefits and possible side effects are considered to be the same as the reference medicine.

Why was Vildagliptin/Metformin approved?

It was concluded that, Vildagliptin/Metformin has been shown to be bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Vildagliptin/Metformin?

As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Vildagliptin/Metformin. The RMP details the important risks of Vildagliptin/Metformin, how these risks can be minimised, any uncertainties about Vildagliptin/Metformin (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Vildagliptin/Metformin:

Summary of safety Concerns	
Important identified risks	• Drug-induced liver injury (IDLI) • Acute pancreatitis • Lactic acidosis
Important potential risks	• Muscle events/myopathy/rhabdomyolysis in particular with current statin use (events of myalgia excluded)
Missing information	• None

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Vildagliptin/Metformin are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Vildagliptin/Metformin

A marketing authorisation for Vildagliptin/Metformin was granted in the United Kingdom (UK) on 29 July 2025.

The full PAR for Vildagliptin/Metformin follows this summary.

This summary was last updated in September 2025.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Vildagliptin/Metformin 50mg/1000mg film-coated tablets (PL 55863/0076) could be approved.

Vildagliptin/Metformin tablets are indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus:

- in patients who are inadequately controlled with metformin hydrochloride alone.
- in patients who are already being treated with the combination of vildagliptin and metformin hydrochloride, as separate tablets.
- in combination with other medicinal products for the treatment of diabetes, when these do not provide adequate glycaemic control (patients should refer to SmPC sections 4.4, 4.5 and 5.1 for available data on different combinations).

Vildagliptin/Metformin combines two antihyperglycaemic agents with complimentary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: vildagliptin, a member of the islet enhancer class, and metformin hydrochloride, a member of the biguanide class.

Vildagliptin, a member of the islet enhancer class, is a potent and selective dipeptidyl-peptidase-4 (DPP-4) inhibitor. Metformin acts primarily by decreasing endogenous hepatic glucose production.

This application was approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as a generic medicine of a suitable originator medicinal product, Eucreas 50 mg / 1000 mg film-coated tablets that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product.

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product. The bioequivalence study was conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Advice was sought from the Commission of Human Medicines (CHM) on 27 June 2024 on grounds relating to quality, safety and efficacy. Following provision of additional data the CHM were reassured on the quality of the product.

A marketing authorisation for Vildagliptin/Metformin was granted in the United Kingdom (UK) on 29 July 2025.

II QUALITY ASPECTS

II.1 Introduction

The active substances are vildagliptin and metformin hydrochloride.
Each Vildagliptin/Metformin 50mg/1000mg film-coated tablets contains 50 mg vildagliptin and 1000 mg metformin hydrochloride (corresponding to 780 mg of metformin).

The other ingredients are:
- Tablet core: Cellulose, microcrystalline (E460), povidone, hydroxypropyl cellulose (E463), magnesium stearate (E470b), ethanol (96 percent).
- Film-coating: Polyvinyl alcohol-part hydrolysed (E1203), talc (E553b), titanium dioxide (E171), glyceryl monocaprylocaprate, sodium laurylsulphate, iron oxide yellow (E172).

The finished product is packaged in Aluminium/Aluminium blister packs containing 10, 30, 60, 120, 180 or 360 film-coated tablets and in multi-packs containing 120 (2x60), 180 (3x60) or 360 (6x60) film-coated tablets.

Not all pack sizes may be marketed.

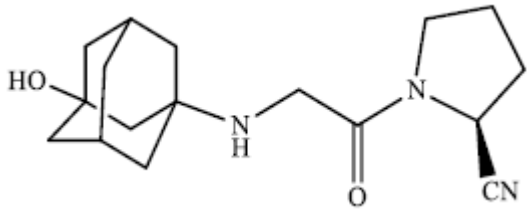
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCES

rINN: vildagliptin

Chemical Name: (2S)-1-[2-[(3-hydroxy-1-adamantyl)amino]-acetyl]pyrrolidine-2-carbonitrile

Molecular Formula: $C_{17}H_{25}N_3O_2$



Chemical Structure:

Molecular Weight: 303.40 g/mol

Appearance: White to off white crystalline powder

Solubility: Freely soluble in methanol, sparingly soluble in Isopropyl alcohol and insoluble in n-Hexane. And freely soluble in Dichloromethane, and in water and sparingly soluble in Acetonitrile.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

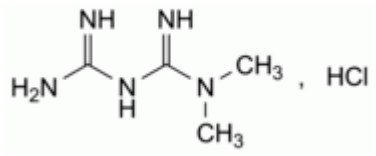
An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant

specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

rINN: metformin hydrochloride
Chemical Name: 1,1-Dimethylbiguanide hydrochloride
Molecular Formula: $C_4H_{12}ClN_5$



Chemical Structure:
Molecular Weight: 165.6 g/mol
Appearance: White or almost white crystals
Solubility: Freely soluble in water, slightly soluble in ethanol (96 per cent), practically insoluble in acetone and in methylene chloride.

Metformin hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development
A satisfactory account of the pharmaceutical development was provided.

Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product
A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications
The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years, with the storage conditions "Store in the original package in order to protect from moisture", is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of vildagliptin & metformin hydrochloride are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for this application.

III.4 Toxicology
No new toxicology data were provided, and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment
A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the application is for a generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the marketing authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisation was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of vildagliptin & metformin hydrochloride is well-known. With the exception of data from a single bioequivalence study undertaken, no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this study is, thus, satisfactory.

IV. 2 Pharmacokinetics

In support of the application, the applicant submitted the following:

Study 1:

This study was an open label, balanced, randomised, two-treatment, two-sequence, two-period, cross-over, single-dose, oral bioequivalence study comparing Vildagliptin/Metformin Hydrochloride Tablets 50 mg/1000 mg (test product) with Eucreas® 50 mg/1000 mg film-coated tablets (reference product) in healthy, adult, human subjects under fed conditions.

In each study period, subjects were administered a single dose of either the test or reference product after an overnight fast of at least 10 hours. Subjects consumed a standard high fat, high calorie breakfast within 30 minutes prior to drug administration. Blood samples were taken pre-dose and up to 36 hours post dose, with a washout period of 7 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Vildagliptin

Parameter (Unit)	(Ln-transformed) Geometric Least Square Mean			90% Confidence Interval
	Test Product (T)	Reference Product (R)	Ratio (T/R)%	
Cmax (ng/mL)	146.1801	155.1932	94.19	85.67-103.57
AUC_{0-t} (hr.ng/mL)	1008.3665	1015.5290	99.29	96.30-102.38

Metformin Hydrochloride

Parameter (Unit)	(Ln-transformed) Geometric Least Square Mean			90% Confidence Interval
	Test Product (T)	Reference Product (R)	Ratio (T/R)%	
Cmax (ng/mL)	1560.6649	1629.7125	95.76	90.36-101.49
AUC_{0-t} (hr.ng/mL)	17818.0739	17933.7965	99.35	96.45-102.34

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

IV.3 Pharmacodynamics
No new pharmacodynamic data were submitted for this application and none were required.

IV.4 Clinical efficacy
No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety
The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

IV.6 Risk Management Plan (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects
The grant of a marketing authorisation was recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with vildagliptin & metformin hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	Scope	Product information affected	Date of grant	Outcome	Assessment report attached Y/N